DEPARTMENT OF VETERANS AFFAIRS OFFICE OF RESEARCH AND DEVELOPMENT'S PAIN PORTFOLIO

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It is an exciting time for pain research at the Department of Veterans Affairs (VA). In the seven years that I have been a Scientific Program Manager in the Rehabilitation Research and Development Service in the Office of Research and Development (ORD), I have witnessed an increase in the number of projects and funded investigators within VA's pain portfolio. In 2009, there were approximately 57 projects on pain research. In July 2015, the number of projects was 109, and importantly, the investment in pain research almost tripled within this time span. This change can be attributed to the increased interest in pain research within VA's scientific and clinical communities brought about by the unique chronic pain management needs of Veterans returning from Iraq and Afghanistan and the collaborative effort between VA's pain research community and ORD to spotlight pain research. Pain research in ORD appropriately spans the translational research spectrum and includes basic/foundational research mainly in animal models, epidemiology to determine the distribution of various painful conditions in the VA, pain diagnosis, management and treatment of pain, underlying causes of chronic pain including the transition from the acute to chronic state, adverse events associated with pain management, and health services-level research. This editorial covers a fraction of the innovative and unique areas of pain research being conducted at the VA and the important role VA researchers play in the pain community, as evidenced by VA participation in the Interagency Pain Research Coordinating Committee (IPRCC) National Pain Strategy (NPS).

VA's research programs are unique entities, serving as platforms and resources for the research community and the Veterans we serve.

- Pain management: The challenge of treating Veterans with chronic pain and coexisting conditions has sparked an interest in how to care for these individuals effectively. Team-based integrative approaches play up to VA's strengths as a healthcare system and include the clinicians who see Veterans in the clinic, who also conduct basic up to health services research. This is reflected in the high number of treatment-related projects (n = 46) examining the effectiveness of exercise and activity; complementary approaches, including electroceuticals (e.g., transcranial magnetic stimulation) and yoga; and testing different formulations of drug therapies focused not only on pain but also on coexisting conditions, including posttraumatic stress disorder (PTSD), depression, sleep, and substance use disorders. The emphasis of treatment includes reduced dependence on opioids as "go to" drugs and examining alternate forms of pain management, putting the Veteran in the driver's seat in managing the painful condition.
- Comparative-effectiveness research: Comparative-effectiveness studies emphasize the importance of "evidence-based practice" and "practice-based evidence" results and are reality checks as to what treatments should be effective and what treatments actually are effective. These types of studies are unique to healthcare systems and aim to improve the delivery of care and maximize patient satisfaction while being cost-effective. It is an area of research well-suited to the VA and an area in which the VA Health Services researchers are leaders in the field. Results from these studies change the way care is delivered at the VA. An example of evidence-based practice research is the adoption of acupuncture for chronic low back pain at the VA, while an example of practice-based evidence research is the ongoing assessment of the Stepped Care Model for pain management. In this case, results recommend the rearrangement of "steps" to make the process more efficient and effective, including rotating the clinicians versus having the patient rotate through the

"steps." Comparative-effectiveness studies are an ideal way to determine best practices that benefit the Veteran.

- Precision medicine: Everyone is talking about precision medicine, but VA pain researchers and clinicians are actually "walking the walk." The Institute of Medicine (IOM) prominently mentioned VA's Stepped Care/Patient Aligned Care Teams (PACTs) as a model for pain management, which includes the patient as a member of the pain management team, thus ensuring individualized treatment, patient participation, and adherence to the treatment plan that they helped develop. Another emerging area of personalized pain management is the screening of individuals with neuropathic pain for mutations in sodium channel dysfunction. Neuropathic pain caused by disease or injury results in alteration in sodium channel function. Genetic mutations in sodium channels result in a gain of function or loss of function with a concomitant change in sensitivity to painful stimuli. This genetic screening approach has been effective in determining who will respond to sodium channel antagonists and the subsequent alleviation of pain in genetic conditions such as erythromelalgia. It is hoped that the technique can be extended to other neuropathic painful conditions, including diabetes and spinal cord injury.
- Pain diagnosis/testing: Pain research occurs in the least likely of places, including the field of regenerative medicine. VA researchers are incorporating pain measurements following the transplantation of ex vivo engineered tissues and cells for joint replacement and spinal cord injury to demonstrate safety and lack of adverse side effects, namely pain. Tissue engineering for musculoskeletal and neurological disorders is a viable alternative if the transplanted tissue does not produce or exacerbate already existing pain. Screening for pain early on in the research and development process decreases the chances that a cell therapy that does not alleviate pain or creates pain will advance to costlier larger animal models or human trials.
- Unique programs: Musculoskeletal pain as a result of Active Duty is often chronic and ranks among the highest in terms of clinic visits. The Musculoskeletal Cohort is a longitudinal project tracking Veterans living with musculoskeletal pain of various etiologies, including osteoarthritis, joint pain, back and neck pain, nerve compression, and other painful conditions originating from a musculoskeletal origin. The Musculoskeletal Cohort is providing VA researchers with data on the occurrence, treatment, and screening of pain; presence of coexisting conditions; and cost of musculoskeletal pain care. Such data can then be analyzed to determine what works and what does not work, and for whom, thus streamlining the process of pain management in the clinic. These data can then help inform PACTs of best practices, falling into alignment with precision medicine.
- Participation on the IPRCC NPS: The IOM recommended the "Secretary of the Department of Health and Human Services (DHHS) should develop a comprehensive population health-level strategy for pain prevention, treatment, management, education, reimbursement, and research that includes specific goals, actions, time frames, and resources." As a result, the IPRCC was tasked by DHHS with developing an NPS as outlined by the IOM. A plan was developed by IPRCC members to accomplish this goal, including an oversight committee and thematic working groups responsible for creating a draft plan for the respective theme. The breadth of expertise provided by VA investigators is evidenced by participation on the working groups and includes Professional Education and Training—Dr. Rollin "Mac" Gallagher; Public Education and Communication—Drs. Keith Humphreys and John Piette; Disparities—Dr. Diana J. Burgess; Service Delivery and Reimbursement—Drs. Karl Lorenz, Patricia Sinnott, and Robert D. Kerns (who also participated as a member of the NPS Oversight Committee); and Population Research—Dr. Joseph L. Goulet. Much time, effort, and collegiality was needed to create a draft of the NPS that was posted on the IPRCC Web site and the Federal Register for public input. The NPS is now in its final stages of amendment prior to final approval by all Federal agencies represented on the IPRCC.

VA's research programs are unique entities, serving as platforms and resources for the research community and the Veterans we serve. The programs I have highlighted are only a small sample of the great research VA investigators are conducting and demonstrates that our investigators are viewed as experts by the pain research community. It can be concluded that we are experiencing "growing pains," but this kind of

pain is good for research, the VA, and Veterans as our researchers continue to break new ground and lead the way in pain research.

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This article and any supplementary material should be cited as follows:
Kusiak AN. Department of Veterans Affairs Office of Research and Development's pain portfolio. J Rehabil Res Dev. 2016;53(1):xi–xiv.
http://dx.doi.org/10.1682/JRRD.2015.08.0149